UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,822	03/19/2004	Lawrence W. Stanton	135/003P	7106

22869 7590 10/12/2007

GERON CORPORATION
230 CONSTITUTION DRIVE
MENLO PARK, CA 94025

EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

MAIL DATE	DELIVERY MODE
10/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/804,822	STANTON ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-28* is/are pending in the application.

4a) Of the above claim(s) *22 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21 and 24-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7-2-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9-11-07 has been entered.

Applicants' amendment filed 9-11-07 has been entered. Claim 21 has been amended. Claims 27 and 28 have been added. Claims 21-28 are pending. Claims 21 and 24-28, and measuring PODXL expression at protein level, are under consideration.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 28 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The phrase "wherein the first set of conditions comprises culturing the cells in the presence of matrix and without a feeder layer" in new claim 28 is considered new matter. The amendment filed 9-11-07 points out support in the specification page 4, lines 20-37, and page 11, lines 21-30. Page 4, lines 20-37, describes the definitions of "pluripotent stem cells", "human

embryonic stem cells" and "undifferentiated". Page 11, lines 21-30, describes preparation of neurons (preNEU) and hepatocyte (preHEP) by using retinoic acid (RA) and DMSO as stimulant, respectively. However, the specification fails to provide sufficient support for "culturing the cells in the presence of matrix and without a feeder layer". Thus, the phrase set forth above is considered new matter.

4. Claims 21 and 24-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 21 and 24-28 are directed to a method for assessing a culture comprising human embryonic stem cells for the presence of undifferentiated cells by measuring PODXL expression level in the culture under a first set of conditions and a second set of conditions, wherein the second set of conditions contains an agent suitable for inducing differentiation of the human embryonic stem cells and the first set of conditions does not have said agent, and a decrease in PODXL level under second set of conditions relative to that of first set of conditions indicates there are more undifferentiated cells in the culture under first set of conditions. Claims 24 and 25 specify the PODXL expression level is measured at the protein level and by antibody assay, respectively. Claim 26 specifies the PODXL expression level is measured using flow cytometry. Claims 27 and 28 specify the first set of conditions comprises culturing the cells in the presence of a feeder layer or a matrix.

The specification discloses a plurality of marker genes that appear to be more abundantly expressed in undifferentiated hES cell lines when compared to that in differentiated hES cell lines (i.e. differentiated hES cell lines that have been induced to differentiate to embryoid body (EB) formation, exposure to retinoid acid to differentiate to neuronal precursor cells, and exposure to DMSO to differentiate to hepatocyte precursor cells). The specification discloses a plurality of marker genes that appear to be less abundantly expressed in undifferentiated hES cell lines as compared to that in differentiated hES cell lines (Examples 1-3, Table 2 and 3). Examples 4, 5 and 8 demonstrate high level expression of PODXL in undifferentiated hES cells and PODXL expression level decreased after growing the undifferentiated hES cells in unconditioned culture medium by real-time PCR assay (mRNA level).

The claims encompass assessing a culture comprising human embryonic stem cells for the presence of undifferentiated cells by measuring PODXL protein expression level in the culture at two different sets of culture conditions. The specification fails to provide adequate guidance and evidence for how to assess the presence of undifferentiated hES cells by measuring PODXL protein expression level. The data shown in Tables 2 and 3, and Examples 4, 5 and 8 of the specification are expression levels of cDNA rather than protein expression levels. It was known in the art that expression levels of cDNA or mRNA do not necessarily correspond to the expression level of protein since there are post-transcription regulation of mRNA and post-translational regulation of protein. Spence et al., 2006 (Molecular Cancer Research, Vol. 4, No. 1, p. 47-60) points out that "[I]n the majority of publications, total mRNA is analyzed, which does not reflect the level of translation of a given transcript. However, experiments in yeast indicate that there is little correlation between mRNA abundance and protein level". It appears

that mRNA level does not necessarily reflect protein level. The specification fails to provide adequate guidance and evidence for whether the expression levels of cDNA or mRNA of PODXL gene at different differentiated stages of the hES cells could be translated into expression levels of PODXL protein. Thus, one skilled in the art at the time of the invention would not know how to use antibody assay to assess or determine the extent of differentiation of hES cells as claimed.

Further, the phrase "a culture comprising human embryonic stem cells" reads on a tissue or organ culture comprising hES cells. The claims encompass assessing the hES cells for the presence of undifferentiated cells in a tissue or organ culture. The specification fails to provide adequate guidance and evidence for how to measure the protein level of PODXL, such as via antibody assay, in the tissue or organ culture, and whether there would be any difference in protein expression level of PODXL between undifferentiated and differentiated hES cells in said tissue or organ culture. There is no evidence of record that shows a decrease in PODXL protein expression level under the presence of a differentiating agent would be indicative of more undifferentiated cells in the tissue or organ culture.

For the reasons set forth above, one skilled in the art at the time of the invention would have to engage in undue experimentation to practice over the full scope of the invention claimed. This is particularly true based upon the nature of the claimed invention, the state of the art, the unpredictability found in the art, the teaching and working examples provided, the level of one of ordinary skill which is high, the amount of experimentation required, and the breadth of the claims.

Applicants argue that Table 4 and Example 8 show Oct 4 mRNA expression corresponds to Oct 4 protein expression. Applicants cite reference Hara and argue that the mRNA expression level of mouse homolog of PODXL corresponds to protein expression level of said mouse homolog of PODXL. No evidence has been provided to support the Office's position with respect to mRNA and protein expression (amendment, p. 4-5). This is not found persuasive because of the reasons set forth above. As discussed above, Spence points out that total mRNA usually does not reflect the level of translation of a given transcript, and there is little correlation between mRNA abundance and protein level in yeast. Oct 4 and PODXL are different genes and they encode different proteins. The expression pattern of Oct 4 cannot be extrapolated into the expression pattern of PODXL. Similarly, mouse and human PODXL genes are different genes that encode different proteins. Although they are homolog of different species, however, expression pattern of mouse PODXL cannot be extrapolated into expression pattern of human PODXL.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.

SHIN-LIN CHEN
PRIMARY EXAMINER